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THE PHYTOCHEMISTRY OF *QUARARIBEA FUNEBRIS*[1]

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In an earlier issue of the *Botanical Museum Leaflets*, the ethnobotany of *Quararibea funebris* (La Llave) Vischer (Bombacaceae) was reviewed. The flowers have been used since pre-Columbian times by the Zapotec Indians of Oaxaca, Mexico as an additive to chocolate drinks and medicinally as an antipyretic, a cough remedy, to control "psychopathic fear" and to regulate the menses (Rosengarten, 1977). There is also some evidence to suggest that they may have been used as an hallucinogen (Wasson, 1982). Other than Rosengarten's report of the presence of alkaloids in these flowers, the chemistry of the genus has not been studied.

In the hands of the phytochemist, the family has not fared much better. Mucilages (Gibbs, 1974), the carbohydrates raffinose and stachyose (Gibbs, 1974; Hegnauer, 1964) and the cyclopropenoid fatty acids obtained from the seed oils have been reported (Bohannen, 1978; Morris and Hall, 1967). In addition to the economically important members of the family (*Ceiba pentandra*, kapok; *Ochroma* spp., balsa wood), the fruits of several genera have been used as food:The durian *Durio zebethinus* Murr. is a very odorous fruit and is claimed to have great rejuvenating powers (Hutchinson, 1967); the young fruits and roasted seeds of *Ceiba aesculifolia* (HBK.) Britt. and Baker, the seeds of *Pachira macrocarpa* (Schlecht. and Cham.) Walp. (Standley,

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[1]This paper is dedicated to my friend and colleague in Natural Products Chemistry of many years, Dr. Ulrich Weiss, National Institutes of Health, in commemoration of his 75th birthday.

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1930) and the fruits of *Quararibea cordata* (H.&B.) García-Barriga and Hernandez are eaten (Hodge, 1960). A decoction of the bark and flowers of *Bombax ellipticum* HBK. is employed as a cough remedy, and the nectar of the flowers is applied to the eyes to relieve inflammation (Standley, 1930). The small stems and twigs of *Q. turbinata* (Schwartz.) Poiret are used in many parts of the West Indies and Central America as frothing sticks called "molinillos," and in some areas it and other species of Quararibea are known as "swizzle stick trees". It is not unlikely that the mucilages present in members of the family account for this use as well as the use as a cough remedy.

The Bombacaceae comprise 31 genera and 225 species distributed among six tribes (Hutchinson, 1967). Quararibea is found in the tribe Matisieae along with seven other genera, including Matisia. The latter genus was considered at one time to be synonymous with Quararibea by some authors (Fisher, 1919; García-Barriga, 1959; Alverson, 1982); but, because of flower morphology, the two are considered by others as separate genera (Schultes, 1957). A possible chemotaxonomic distinction lies in the peculiar odor of all parts of the plants of the genus Quararibea, the flowers being particularly odorous. The odor can be described as a cross between vanilla and linden flowers; some compare it to the odor of slippery elm bark (Standley, 1930) or fenugreek (Record, 1939). However it may be described, it is completely absent in Matisia and thus represents a distinction between the two genera. The genus Quararibea contains 29 species, all of which have this odor: It is so persistent that a specimen collected in 1841 was found still to possess this noticeable aromatic character (Schultes, 1957).

There were, then, several reasons to undertake the complete phytochemical investigation of the flowers of *Quararibea funebris* which is summarized here; experimental details will be published elsewhere.

The milled flowers were extracted first with hexane, then with 95% ethanol. Traditional solvent partition and chromatographic methods were used to separate these extracts into several fractions which were examined individually. The neutral hexane-soluble constituents were unremarkable: a mixture of waxy

hydrocarbons (predominantly C_{25}, C_{27} and C_{29} alkanes), the ethyl esters of linoleic and linolenic acids, and a mixture of C_{29}-C_{31} sterols (chiefly β-sitosterol) esterified with C_{16} and C_{18} fatty acids were obtained. A neutral chloroform fraction yielded, in addition to small amounts of the above compounds, some free fatty acids and the glucosides and glucoside palmitic/oleic acid esters of β-sitosterol and stigmasterol—all known compounds.

It was in the alcohol extract that the interesting chemistry of the plant was revealed. Concentration, partition between aqueous and organic phases at selected pH values, followed by chromatographic separation and crystallization, yielded several compounds. The odor principle was identified as 3-hydroxy-4,5-dimethyl-2(5H)-furanone (IV): the first report of this compound in a plant. It had been recognized previously as a constituent of aged sake formed during the aging process rather than as a constituent of sake itself (Takahashi, 1976); and as a constituent of sugar cane molasses (Tokimoto, 1980). It had been synthesized even earlier in a study of food flavorings (Sulser, 1972) and was found to have one of the lowest threshold values known for food flavoring compounds, perceivable in concentrations as low as 0.01 ppb. It is also attractive to cockroaches, houseflies and ants, and has been described as having the flavor of walnuts. A structurally similar ketone, 2,5-dimethyl-4-hydroxy-3(2H)-furanone, has been reported from pineapple, contributing a "burnt pineapple" note to the overall flavor of the fruit (Rodin, 1965).

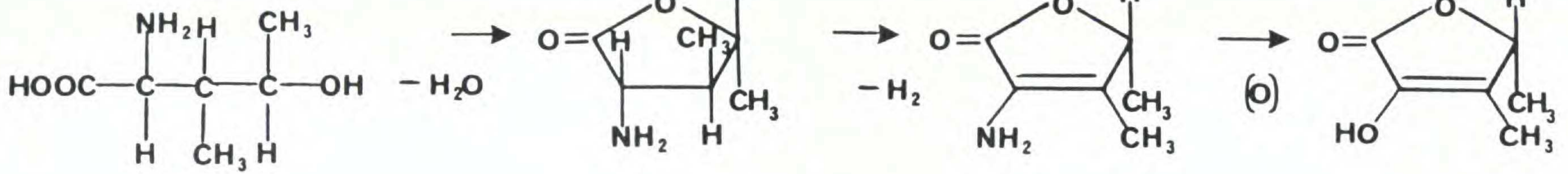
Two closely related aminolactones, 3-amino-4,5-dimethyl-2(5H)-furanone (III) and its saturated analog (II) were also isolated from the flowers and, to our knowledge, are likewise new to the plant kingdom. The presence in *Q. funebris* of these lactones is of more than passing interest in view of a recent publication on the anticonvulsant activity and potential clinical usefulness of a group of alkyl-substituted butyrolactones (Klunk, 1982) structurally related to them. It is not unlikely that some of the folk-medical use of the flowers is referable to these compounds. Further, the hypothermic and behavioral effects reported for γ-hydroxybutyric acid itself (Snead, 1978) suggest that the utilization of *Q. funebris* preparations as antipyretics and possibly as an hallucinogen may not be at all unreasonable. Pharmacological

studies designed to test these hypotheses are planned. Also present, albeit in very small amounts, was an alkaloid of a new structural type which we had named "funebrine" (V) and which represents the first alkaloid to be recorded in the Bombacaceae. It was accompanied by at least two other polar alkaloidal compounds in quantities too small to permit characterization at the present time.

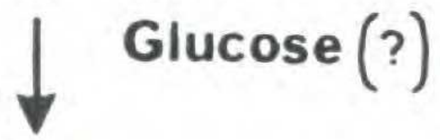
Finally, the isolation of a novel amino acid, 2S,3S,4R-4-hydroxyisoleucine (I) in substantial amounts allowed us to propose a biogenetic scheme for the synthesis by the plant of the above compounds as shown in the accompanying figure. The novelty of this amino acid lies in the fact that it appears to be a diasteriomer new in nature; its epimer, 2S,3R,4R-4-hydroxyisoleucine, had been isolated from fenugreek seed (Fowden, 1973) and was found to be a component of α-amanitin (Wieland, 1968). The fact that I could be converted readily to II was of obvious help in defining the geometry of the other compounds in the series.

Among the non-nitrogenous constituents of the remaining aqueous fractions of the ethanolic extract were rather large quantities of glucose, fructose and sucrose. This leads to the suggestion that the flowers served the additional purpose of sweenening the Zapotec chocolate drinks, inasmuch as sugar cane was not known in the New World until after the Conquest. A small amount of a complex mixture of flavonoids was also present, but no individual compounds were identified.

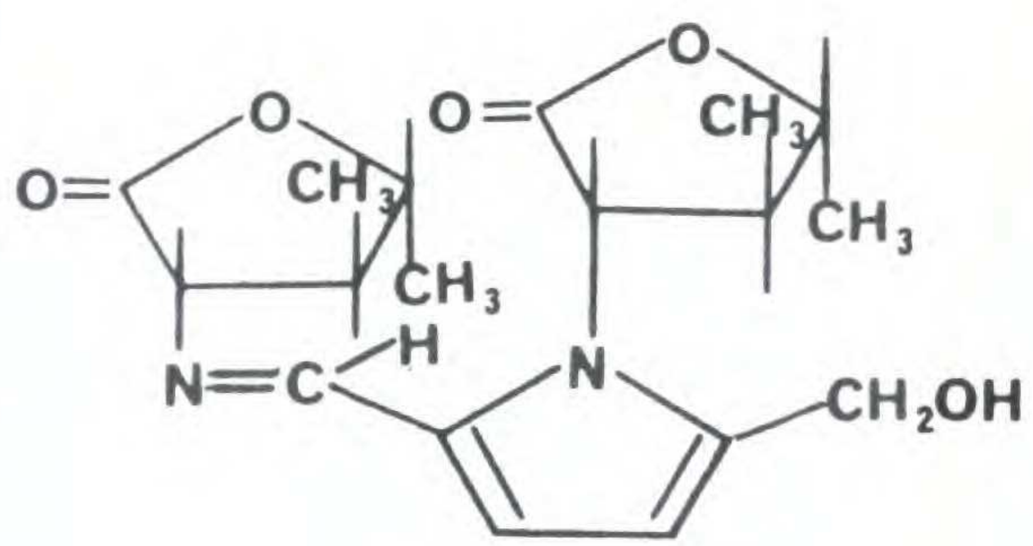
During the course of the study, a small sample of *Quararibea turbinata* leaves became available to us. The chemical profile of these was very similar to that of the *Q. funebris* flowers; compounds I, II and III were identified, the presence of alkaloids was established and compound IV, though not yet isolated and identified, is suspected to be present by reason of the familiar odor of the extracts. We have recently acquired several other species of the *Quararibea/ Matisia* complex and will be interested to learn whether any one or all of these compounds will serve to distinguish the genera in this portion of the Bombacaceae of whether, indeed, they are characteristic of the family.



I II III IV



Glucose (?)



V

FUNEBRINE

In any event, virtually all of the substances isolated and characterized in this study are new to the genus *Quararibea* and to the Bombacaceae, and some of them are new to the plant kingdom itself. Inasmuch as the γ-butyrolactones can act as convulsants and anticonvulsants, and since *Q. funebris* flowers are used medicinally as a sort of anti-anxiety folk remedy—a common side effect of all anticonsulvant drugs is sedation—it seems reasonable to suggest that the lactones isolated in this study may act in a similar way, corroborating once again the wisdom of the early meso-American peoples in their use of biodynamic plants.

We are indebted to Dr. R. Gordon Wasson and Prof. Richard Evans Schultes for making available bulk samples of the flowers of *Quararibea funebris*: representative material of both collections have been deposited as voucher specimens in the Botanical Museum of Harvard University. Dr. José Luis Vivaldi, Department of Natural Resources, Commonwealth of Puerto Rico, has helped us in collecting and identifying the leaves of *Q. turbinata*. To Dr. Schultes we are grateful for his sustained interest in our research.

The voucher specimen on which the final chemical studies were made consisted of dried flowers purchased in the marketplace in Oaxaca, Mexico. Samples have been deposited in the Economic Products Collection in the Botanical Museum of Harvard University. The material was collected by *R.E. Schultes s.n.* in August, 1981.

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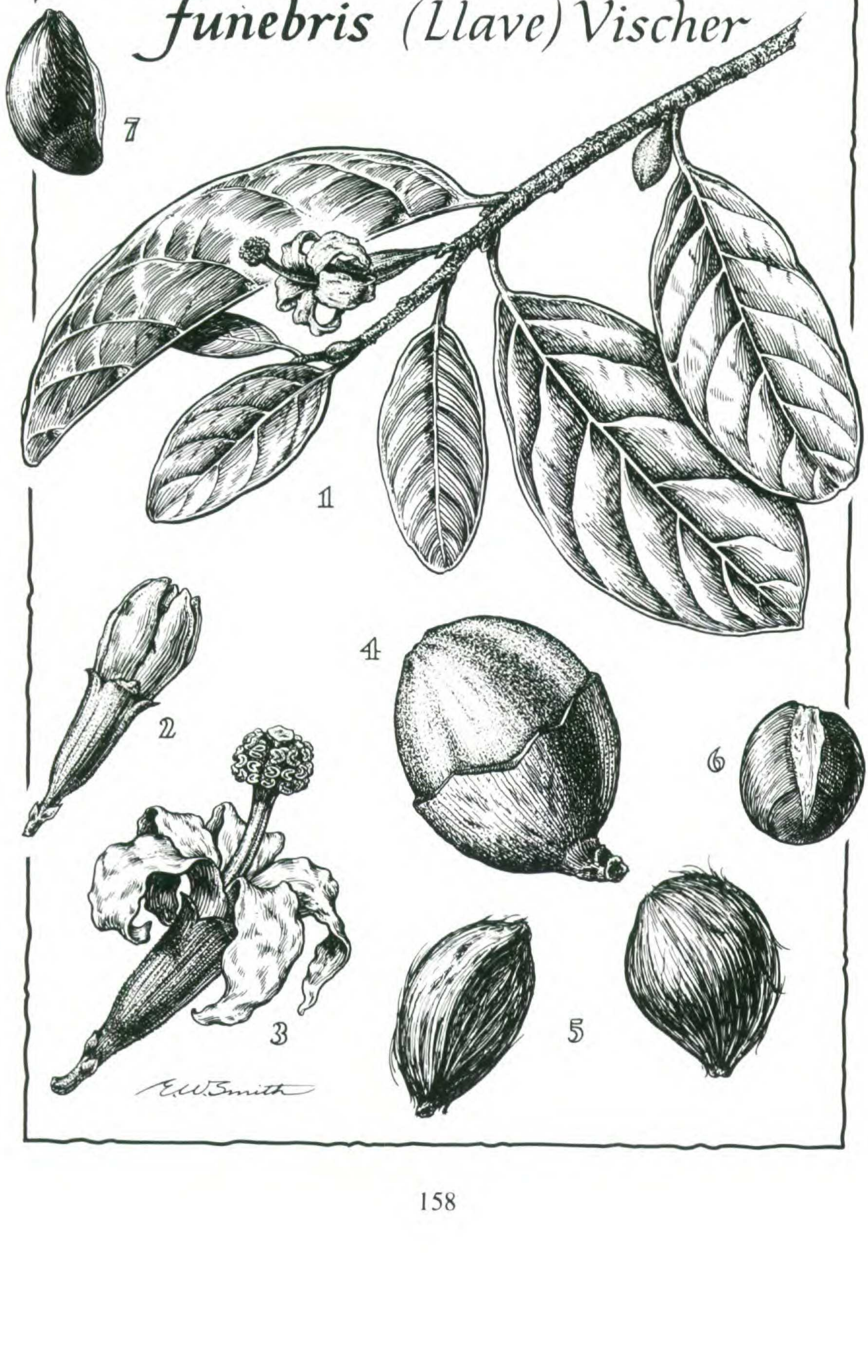
PLATE 19

QUARARIBEA
funebris (Llave) Vischer



E. W. Smith